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Hypercalcemia and acute renal failure indicating peritoneal sarcoidosis

Claude Bachmeyer, MD^a

Nicolas Belaube, MD^b

Valeria Loi, MD^c

Mathieu Gauthé, MD PhD^d

Jean Philippe Haymann, MD PhD^e

^aService de Médecine Interne, Tenon Hospital, (AP-HP), Paris, France

^bService de Maladies Infectieuses, Tenon Hospital, (AP-HP), Paris, France

^cService de Chirurgie Digestive, Saint-Antoine Hospital, (AP-HP), Paris, France

^dService de Médecine Nucléaire, Tenon Hospital, (AP-HP), Paris, France

^eExplorations fonctionnelles Néphrologiques, Tenon Hospital, (AP-HP), Paris, France

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Address correspondence to : Claude Bachmeyer, MD, Service de Médecine Interne, Tenon Hospital (AP-HP), 4, rue de la Chine, 75020 Paris, France

Phone number: 33 1.56 01 60 77; Fax number: 33 1 56 01 70 82

E-mail: claud.bachmeyer@tnn.aphp.fr

To the Editor:

CASE REPORT

An 82-year-old Chinese man with a history of diabetes mellitus and chronic renal failure of undetermined origin (steady-state serum creatinine level 140 $\mu\text{mol/l}$) was referred for fatigue and decreased renal function. The clinical examination was unremarkable. Blood cell count was normal, serum creatinine 253 $\mu\text{mol/L}$ (normal <100) and urea 13.7 mmol/L (normal <6.4), Serum protein electrophoresis and dosage of light chains were normal. Serum ionized calcium was increased at 1.47 mmol/L (normal <1.31), phosphate 1.49 mmol/L (normal <1.31), 1,25-(OH) D_3 70 pg/mL (normal <67), 25-(OH) D_3 40 ng/mL (normal 30-100), parathyroid hormone (PTH) 6.7 ng/L (normal > 8), urine calcium 3.01 mmol/24 h (normal 2.5-7.5). Thoraco-abdominopelvic CT scan with no contrast product showed normal kidney size and no urinary tract obstruction, but hilar lymphadenopathy, micronodules in the upper lobe of right lung, peritoneal nodules and thickening (Figure, A). 2-[^{18}F]FDG PET/CT revealed intense uptake of pleural, pericardial and peritoneal thickening, and of thoracic lymph nodes (Figure, B). Direct search for mycobacteria in sputum and urine, and QuantiFERON Tb Gold Test were negative. Pending explorative laparoscopy for a high suspicion of peritoneal tuberculosis delayed because of Covid19 pandemic conditions, rapid control of serum calcium was obtained under cinacalcet, but fatigue persisted and creatinine level plateaued at 280 $\mu\text{mol/l}$. The explorative laparoscopy revealed diffuse soft and white nodules, 2 -5 mm in diameter, in the peritoneal cavity (Figure, C), histologic examination displaying non-caseating granuloma with negative bacterial, mycobacterial, fungal cultures. Diagnosis of sarcoidosis was established with no other organ involvement, but the patient declined renal biopsy. Treatment with prednisone was given (1 mg/kg/d) tapered over 6 months, associated with isoniazid and rifampicin during 3 months (until the infectious investigations were definitely negative). This allowed cinacalcet withdrawal within

two weeks and return of serum creatinine level to steady level and complete metabolic response on 2-[¹⁸F]FDG PET/CT at six-month follow-up (Figure, D).

DISCUSSION

We report here a case of acute kidney failure and hypercalcemia indicating peritoneal sarcoidosis. Sarcoidosis is a systemic disease of unknown origin characterized by non-caseating epithelioid granulomas, requiring ruling out other granulomatous conditions.¹ Involvement of any organ is reported but mainly lymph nodes, lungs, skin, and eyes. Peritoneal sarcoidosis is rare, often associated with other organ involvement.² Differential diagnosis with peritoneal tuberculosis or carcinomatosis is difficult on clinical features and imaging. Moreover, the association of these conditions is possible.³ Therefore surgery with pathologic examination can be required to establish a definite diagnosis.

Renal involvement of sarcoidosis is usually asymptomatic and consists mainly of granulomatous interstitial nephritis.⁴ In our case, interstitial nephritis and nephrocalcinosis were also possible as no renal biopsy was performed and serum creatinine resumed to previous values at six-month follow-up. Hypercalcemia is a frequent complication of sarcoidosis reported in 2-63% of patients, associated with hypercalciuria in most cases.⁴ It results from uncontrolled synthesis of 1,25-OH D₃ by macrophages responsible for an increased absorption of calcium in the intestine, an increased resorption of calcium in the bone leading to a low PTH value. In our case report, PTH level was indeed low with an unexpected high 1,25-(OH)D₃ level in the setting of acute renal failure suggesting a granulomatous disease.

Treatment of hypercalcemia in patients with sarcoidosis depends on the hypercalcemia level.⁴ Severe hypercalcemia usually requires intravenous rehydration therapy, corticosteroids

(acting by inhibition 1 alpha-hydroxylase activity of macrophages) and bisphosphonates can be associated. Corticosteroids are also indicated in slightly increased hypercalcemia, when systemic symptoms are present and when severe organ involvement is associated. Our report suggests that calcimimetic agents may also be effective in the control of non-PTH dependent hypercalcemia pending specific treatment.

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Legend of figures

Figure (A) Abdominal CT scan without contrast showing peritoneal thickening (star) and small peritoneal nodules (arrow). (B) 2-[¹⁸F]FDG PET/CT showing increased uptake of the tracer at pleural, pericardial and peritoneal hypermetabolic sites and hilar lymphadenopathy. (C) Diffuse soft and white peritoneal nodules demonstrated on laparoscopy. (D) Complete metabolic response on 2-[¹⁸F]FDG PET/CT at six-month follow-up

